

# **SUPPLEMENTAL MATERIAL**

**Table S1. Propensity Score Model Results of Probability of Using Any  $\beta$ -blockers**

Parameter	Estimate	Odds Ratios	95% CI		P value
			Lower	Upper	
<b>Age, per year</b>	-0.013	0.987	0.986	0.988	<.0001
<b>Male</b>	-0.2135	0.808	0.79	0.826	<.0001
<b>Year of Index Date</b>					
<b>2000</b>		1			
<b>2001</b>	-0.121	0.886	0.823	0.954	0.0014
<b>2002</b>	-0.1048	0.901	0.838	0.967	0.0041
<b>2003</b>	-0.1156	0.891	0.831	0.955	0.0012
<b>2004</b>	-0.0917	0.912	0.852	0.977	0.0083
<b>2005</b>	-0.0486	0.953	0.89	1.019	0.1585
<b>2006</b>	-0.0903	0.914	0.854	0.978	0.0093
<b>2007</b>	-0.0777	0.925	0.865	0.99	0.0247
<b>2008</b>	-0.115	0.891	0.833	0.954	0.0009
<b>2009</b>	-0.1223	0.885	0.826	0.947	0.0004
<b>2010</b>	-0.1219	0.885	0.827	0.948	0.0005
<b>2011</b>	-0.103	0.902	0.842	0.967	0.0035
<b>Month of Index Date</b>					
<b>January</b>		1			
<b>February</b>	-0.0006	0.999	0.946	1.056	0.984
<b>March</b>	0.0324	1.033	0.981	1.088	0.2202
<b>April</b>	0.0461	1.047	0.994	1.103	0.0837
<b>May</b>	-0.014	0.986	0.936	1.039	0.5997
<b>June</b>	-0.0283	0.972	0.922	1.025	0.2948
<b>July</b>	-0.0316	0.969	0.92	1.02	0.231
<b>August</b>	-0.0498	0.951	0.902	1.003	0.0659
<b>September</b>	-0.0584	0.943	0.895	0.994	0.0304
<b>October</b>	0.0209	1.021	0.97	1.075	0.4257
<b>November</b>	-0.033	0.968	0.919	1.019	0.2124
<b>December</b>	0.0015	1.002	0.951	1.055	0.9537
<b>Monthly income, NT\$</b>					
<b>Dependent</b>		1			
<b>&lt;19,100</b>	-0.0387	0.962	0.934	0.991	0.0108
<b>19,100–41,999</b>	-0.1063	0.899	0.877	0.922	<.0001
<b>≥42,000</b>	-0.0763	0.927	0.88	0.975	0.0037
<b>Urbanization<sup>a</sup></b>					
<b>Level 1</b>		1			

<b>Level 2</b>	-0.0154	0.985	0.963	1.007	0.1768
<b>Level 3</b>	-0.0794	0.924	0.878	0.972	0.0021
<b>Level 4 (rural area)</b>	-0.127	0.881	0.788	0.984	0.025
<b>Outpatient Visits, in the past one year</b>					
<b>0–5 visits</b>		1			
<b>6–10 visits</b>	0.8204	2.271	2.042	2.527	<.0001
<b>11–15 visits</b>	1.1103	3.035	2.743	3.359	<.0001
<b>&gt;15 visits</b>	1.414	4.113	3.735	4.529	<.0001
<b>Charlson Comorbidity Index Score<sup>b</sup></b>	-0.0317	0.969	0.963	0.975	<.0001
<b>Adapted Diabetes Complications Severity Index score<sup>c</sup></b>	-0.0015	0.998	0.991	1.006	0.6717
<b>Duration of diabetes, months</b>	-0.001	0.999	0.999	0.999	<.0001
<b>Revised Cardiac Risk Index</b>					
<b>High-risk surgery</b>	-0.0453	0.956	0.925	0.987	0.0066
<b>Ischemia heart disease</b>	0.3219	1.38	1.346	1.414	<.0001
<b>Cerebrovascular disease</b>	-0.0375	0.963	0.863	1.075	0.5025
<b>Heart failure</b>	-0.0256	0.975	0.943	1.007	0.129
<b>Renal insufficiency</b>	-0.0034	0.997	0.915	1.086	0.9383
<b>Type of procedure</b>					
<b>Vascular</b>	0.1437	1.155	1.097	1.215	<.0001
<b>Orthopedic</b>	-0.1806	0.835	0.813	0.857	<.0001
<b>Abdominal</b>	-0.0135	0.987	0.955	1.019	0.4088
<b>Thoracic</b>	-0.1346	0.874	0.808	0.945	0.0007
<b>Other</b>		1			
<b>Anti-diabetic drugs</b>					
<b>Acarbose inhibits enzymes</b>	0.0496	1.051	0.996	1.109	0.0711
<b>Sulfonylurea</b>	-0.0006	0.999	0.972	1.028	0.9688
<b>Insulin</b>	-0.0189	0.981	0.924	1.042	0.5343
<b>Metformin</b>	0.0193	1.019	0.992	1.047	0.1636
<b>Thiazolidinediones</b>	-0.0149	0.985	0.932	1.042	0.5994
<b>Glinide</b>	0.1165	1.124	1.059	1.192	0.0001
<b>Dipeptidyl peptidase-4 inhibitor</b>	0.192	1.212	1.105	1.329	<.0001
<b>Anti-hypertensive drug</b>					
<b>Alpha-blocker</b>	0.199	1.22	1.165	1.278	<.0001
<b>Calcium channel blocker</b>	0.6757	1.965	1.921	2.01	<.0001
<b>Diuretics</b>	0.5486	1.731	1.686	1.777	<.0001
<b>ACEI/ARB</b>	0.2849	1.33	1.298	1.362	<.0001

<b>Other anti-hypertensive drug</b>	0.3421	1.408	1.322	1.5	<.0001
<b>Other concomitant medications</b>					
<b>Aspirin</b>	0.5399	1.716	1.671	1.762	<.0001
<b>Clopidogrel</b>	0.552	1.737	1.618	1.864	<.0001
<b>Ticlopidine</b>	0.5634	1.757	1.597	1.932	<.0001
<b>Warfarin</b>	0.2744	1.316	1.184	1.462	<.0001
<b>Dipyridamole</b>	0.2663	1.305	1.255	1.357	<.0001
<b>Nitrate</b>	0.4043	1.498	1.439	1.56	<.0001
<b>Statin</b>	0.1323	1.141	1.109	1.175	<.0001
<b>Comorbidities</b>					
<b>Hypertension</b>	1.1722	3.229	3.114	3.349	<.0001
<b>Peripheral vascular disease</b>	0.0415	1.042	0.998	1.088	0.0588
<b>Atrial fibrillation</b>	-0.0201	0.98	0.93	1.033	0.4554
<b>Dyslipidemia</b>	0.0754	1.078	1.053	1.104	<.0001
<b>Valvular heart disease</b>	0.2002	1.222	1.183	1.262	<.0001
<b>Cancer</b>	0.0634	1.065	1.031	1.101	0.0002
<b>Autoimmune disease</b>	0.1246	1.133	1.079	1.189	<.0001
<b>Physical limitation</b>	-0.1069	0.899	0.867	0.932	<.0001

<sup>a</sup>Urbanization levels in Taiwan are divided into four strata according to the Taiwan National Health Research Institute publications. Level 1 designates the most urbanized areas, and level 4 designates the least urbanized areas.

<sup>b</sup>Charlson Comorbidity Index score is used to determine overall systemic health. With each increased level of CCI score, there are stepwise increases in the cumulative mortality.

<sup>c</sup>Adapted Diabetes Complications Severity Index is a 13-point scale from 7 complication categories: retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral vascular disease, and metabolic, ranging from each complication. Each complication produced a numeric score ranging from 0 to 2 (0 = no abnormality, 1 = some abnormality, 2 = severe abnormality)

*Abbreviations:* CI, confidence interval; NT dollars, new Taiwan dollars; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker.

**Table S2. Baseline Characteristics of Patients with Diabetes Mellitus Before Propensity Score-Matching**

<b>Characteristics</b>	<b>β blockade cohort</b>	<b>Control cohort</b>	<b>StD<sup>†</sup></b>
<b>Patient (no.)</b>	51668	230539	
<b>Mean age (SD), year</b>	64.3 (12.20)	61.8 (13.9)	0.186
<b>Male</b>	24,203 (46.8)	122,821 (53.3)	-0.129
<b>Monthly income, NT\$</b>			
<b>Dependent</b>	17,643 (34.1)	68,425 (29.7)	0.096
<b>&lt;19,100</b>	10,780 (20.9)	48,473 (21.0)	-0.004
<b>19,100–41,999</b>	20,174 (39.0)	99,618 (43.2)	-0.063
<b>≥42,000</b>	2,531 (4.9)	14,023 (6.1)	-0.052
<b>Urbanization<sup>§</sup></b>			
<b>Level 1</b>	17,882 (34.6)	79,688 (34.6)	0.001
<b>Level 2</b>	30,893 (59.8)	137,004 (59.4)	0.007
<b>Level 3</b>	2,444 (4.7)	11,637 (5.0)	-0.015
<b>Level 4 (rural area)</b>	449 (0.9)	2,210 (1.0)	-0.009
<b>Outpatient Visits, in the past one year</b>			
<b>0–5 visits</b>	456 (0.9)	17,591 (7.6)	-0.339
<b>6–10 visits</b>	1,918 (3.7)	20,983 (9.1)	-0.221
<b>11–15 visits</b>	4,019 (7.8)	26,609 (11.5)	-0.128
<b>&gt;15 visits</b>	45,275 (87.6)	165,356 (71.7)	0.403
<b>Charlson Comorbidity Index Score<sup>‡</sup> (SD)</b>	7.5 (3.1)	6.6 (3.3)	0.286
<b>Adapted Diabetes Complications Severity Index score<sup>¶</sup> (SD)</b>	2.9 (2.5)	2.0 (2.1)	0.392
<b>Duration of diabetes mellitus, months (SD)</b>	47.5 (38.5)	43.5 (37.8)	0.106
<b>Revised Cardiac Risk Index</b>			
<b>High-risk surgery</b>	14,200 (27.5)	53,476 (23.2)	0.099
<b>Ischemia heart disease</b>	29,695 (57.5)	82,340 (35.7)	0.447
<b>Cerebrovascular disease</b>	483 (0.9)	1,651 (0.7)	0.024
<b>Heart failure</b>	10,592 (20.5)	27,812 (12.1)	0.230
<b>Renal insufficiency</b>	800 (1.5)	2,833 (1.2)	0.027
<b>Type of procedure</b>			
<b>Vascular</b>	4,998 (9.7)	11,896 (5.2)	0.173
<b>Orthopedic</b>	13,694 (26.5)	71,133 (30.9)	-0.096

<b>Abdominal</b>	8,461 (16.4)	41,264 (17.9)	-0.040
<b>Thoracic</b>	1,059 (2.0)	5,572 (2.4)	-0.025
<b>Other</b>	23,456 (45.4)	100,674 (43.7)	0.035
<b>Concomitant medications</b>			
<b>Anti-diabetic drugs</b>			
<b>Acarbose inhibits enzymes</b>	2,324 (4.5)	6,447 (2.8)	0.091
<b>Sulfonylurea</b>	12,631 (24.4)	42,550 (18.5)	0.146
<b>Insulin</b>	1,846 (3.6)	6,337 (2.7)	0.047
<b>Metformin</b>	14,266 (27.6)	48,466 (21.0)	0.154
<b>Thiazolidinediones</b>	2,114 (4.1)	6,680 (2.9)	0.065
<b>Glinide</b>	1,998 (3.9)	4,934 (2.1)	0.101
<b>Dipeptidyl peptidase-4 inhibitor</b>	798 (1.5)	1,904 (0.8)	0.066
<b>Anti-hypertensive drug</b>			
<b>Alpha-blocker</b>	3,443 (6.7)	8,132 (3.5)	0.143
<b>ACEI or ARB</b>	21,214 (41.1)	42,622 (18.5)	
<b>Calcium channel blocker</b>	26,582 (51.4)	47,921 (20.8)	0.674
<b>Diuretics</b>	14,863 (28.8)	26,816 (11.6)	0.437
<b>Other anti-hypertensive drug</b>	1,806 (3.5)	3,277 (1.4)	0.134
<b>Aspirin</b>	15,211 (29.4)	25,584 (11.1)	0.469
<b>Clopidogrel</b>	1,664 (3.2)	2,279 (1.0)	0.156
<b>Ticlopidine</b>	820 (1.6)	1,282 (0.6)	0.100
<b>Warfarin</b>	645 (1.2)	1,230 (0.5)	0.076
<b>Dipyridamole</b>	4,975 (9.6)	10,034 (4.4)	0.208
<b>Nitrate</b>	6,027 (11.7)	76,056 (33.0)	0.322
<b>Statin</b>	11,078 (21.4)	27,948 (12.1)	0.251
<b>Comorbidities</b>			
<b>Hypertension</b>	47,340 (91.6)	146,317 (63.5)	0.717
<b>Peripheral vascular disease</b>	3,613 (7.0)	12,293 (5.3)	0.069
<b>Atrial fibrillation</b>	2,715 (5.3)	6,957 (3.0)	0.113
<b>Dyslipidemia</b>	33,501 (64.8)	122,659 (53.2)	0.238
<b>Valvular heart disease</b>	7,775 (15.0)	19,513 (8.5)	0.205
<b>Cancer</b>	8,088 (15.7)	34,450 (14.9)	0.020
<b>Autoimmune disease</b>	2,648 (5.1)	9,131 (4.0)	0.056
<b>Physical limitation</b>	5,373 (10.4)	19,408 (8.4)	0.068
<b>Propensity score (SD)</b>	0.30 (0.16)	0.16 (0.13)	0.987

\* All data were described as number (%), except mean age and propensity score.

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† Imbalance defined as absolute value greater than 0.015

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‡Charlson Comorbidity Index score is used to determine overall systemic health. With each increased level of CCI score, there are stepwise increases in the cumulative mortality.

¶Adapted Diabetes Complications Severity Index is a 13-point scale from 7 complication categories: retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral vascular disease, and metabolic, ranging from each complication. Each complication produced a numeric score ranging from 0 to 2 (0 = no abnormality, 1 = some abnormality, 2 = severe abnormality).

*Abbreviations:* StD, Standardized difference; SD, standard deviation; NT\$, new Taiwan dollars; ACEI, angiotensin-converting-enzyme inhibitors; ARB, Angiotensin II receptor blockers.

**Table S3. Odds Ratios of Effect of Perioperative  $\beta$  blockade on Mortality among Patients with Diabetes Mellitus Undergoing Noncardiac surgery Before Propensity Score Matching**

	No. of Event/ No. of Patients (%)	Adjusted* Odds Ratio (95% CI)	P Value
<b>In hospital Mortality</b>			
$\beta$ blockade non-user	6925/230539	Reference	
All $\beta$ blockade	1546/51668	0.89 0.84-0.95	<0.001
Atenolol, bisoprolol, carvedilol, and metoprolol	906/32662	0.80 0.74-0.87	<0.001
Others $\beta$ blockade	640/19006	1.03 0.95-1.13	0.475
<b>30-day Mortality</b>			
$\beta$ blockade non-user	9920/230539	Reference	
All $\beta$ blockade	2145/51668	0.87 0.83-0.92	<0.001
Atenolol, bisoprolol, carvedilol, and metoprolol	1280/32662	0.81 0.76-0.87	<0.001
Others $\beta$ blockade	865/19006	0.97 0.90-1.05	0.488

\* Adjusted all covariates listed in Table 1.

Abbreviations: CI, confidence interval.

**Table S4. Subgroup Analysis of Risks of Using Any  $\beta$ -blockers on 30-day Mortality among Patients with Diabetes Mellitus Undergoing Noncardiac Surgery**

<b>Characteristic</b>	<b>Odds Ratios (95% CI)</b>	<b><i>P</i> Value</b>	<b>Interaction <i>P</i> Value</b>
<b>Sex</b>			
<b>Male</b>	0.820 (0.755-0.889)	<0.001	0.524
<b>Female</b>	0.852 (0.781-0.929)	<0.001	
<b>Age</b>			
<b>20-64 years</b>	0.942 (0.846-1.048)	0.274	0.007
<b><math>\geq 65</math> years</b>	0.788 (0.733-0.847)	<0.001	
<b>Hypertension</b>			
<b>Yes</b>	0.813 (0.764-0.865)	<0.001	0.003
<b>No</b>	1.147 (0.926-1.421)	0.210	
<b>Dyslipidemia</b>			
<b>Yes</b>	0.873 (0.804-0.947)	0.001	0.116
<b>No</b>	0.793 (0.727-0.865)	<0.001	
<b>Cerebrovascular disease</b>			
<b>Yes</b>	0.883 (0.546-1.428)	0.611	0.819
<b>No</b>	0.834 (0.786-0.885)	<0.001	
<b>Myocardial infarction</b>			
<b>Yes</b>	0.807 (0.748-0.870)	<0.001	0.148
<b>No</b>	0.883 (0.801-0.973)	0.012	
<b>Heart failure</b>			
<b>Yes</b>	0.770 (0.698-0.850)	<0.001	0.048
<b>No</b>	0.873 (0.809-0.941)	<0.001	
<b>Chronic kidney disease</b>			
<b>Yes</b>	1.107 (0.701-1.746)	0.663	0.221
<b>No</b>	0.831 (0.782-0.882)	<0.001	
<b>Revised cardiac risk index</b>			
<b>1</b>	0.905 (0.767-1.068)	0.239	0.106
<b>2</b>	0.838 (0.755-0.930)	0.001	
<b>3</b>	0.867 (0.781-0.963)	0.008	
<b><math>\geq 4</math></b>	0.719 (0.628-0.823)	<0.001	
<b>Vascular surgery</b>			
<b>Yes</b>	0.744 (0.675-0.821)	<0.001	0.044
<b>No</b>	0.847 (0.783-0.917)	<0.001	
<b>Year of index date</b>			
<b>2000-2003</b>	0.783 (0.688-0.892)	<0.001	0.116

<b>2004-2007</b>	0.796 (0.722-0.878)	<0.001
<b>2008-2011</b>	0.899 (0.820-0.985)	0.022

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Abbreviations: CI, confidence interval.

**Figure S1. The Distribution of the Propensity Scores Before and After Propensity Score Matching**

